



TO CORRELATE eGFR IN PATIENTS WITH DIABETIC FOOT ULCER

Karthik S¹, Dr. A Rekha², Raghavendra Rao M.V³

¹ IVth year MBBS, Saveetha Medical College and Hospital, Thandalam, Kancheepuram, Chennai, India.

² Professor, Department of General Surgery, Saveetha Medical College and Hospital, Thandalam, Kancheepuram, Chennai, India.

³ Scientist-Emeritus, Director, Central Research Laboratory, Apollo Institute of Medical Sciences and Research, Jubilee Hills, Hyderabad, T S, India.

ABSTRACT

Diabetes mellitus is a metabolic disease condition where the control of glucose levels in blood is inadequate. Estimated Glomerular filtration rate (GFR) refers to the rate of flow of the fluid that is filtered through the glomerulus in the kidney, which is estimated by some formulas. Diabetic patients tend to develop ulceration of the foot due to peripheral sensory neuropathy. So, preventing and managing Chronic kidney disease (CKD) is also important in patients with diabetic foot ulcer, along with prevention of amputations.

Aim of the study:

- (a) To look at the demographics of the patients with diabetic foot ulcer
- (b) To see the extent of the injury in foot- clinical and amputation status
- (c) To study the oxygen saturation levels in the periphery
- (d) To calculate the eGFR in patients with diabetic foot ulcer

Materials and Methods:

- (a) It's a prospective study conducted on 80 patients with diabetic foot ulcer who attended the Outpatient Department of Surgery in Saveetha Medical College and Hospital, a tertiary care hospital in Chennai, India.
- (b) We conducted clinical and radiological examination
- (c) We calculated eGFR through a predetermined scoring system

Result: Out of the 80 patients, around 70 patients were found to be above the age of 50. Most number of patients were belonging to stage 3 (40%) of the Wagner's diabetic foot ulcer classification. About 59 patients were found to have minimum of 5 years of diabetic history. 17 patients had high serum creatinine levels. Around 65 patients in total were found to be anaemic. Around 55 patients had high HbA1C values. Mean HbA1C was found to be 10.2 ± 2.83 mg/dl. Maximum number of patients (58.7%) belonged to stage 1 CKD based on the eGFR levels. 17 patients had high serum creatinine levels. About 45% patients underwent amputation. About 28 patients had peripheral SpO₂ less than 97. Around 21 of them had gangrenous diabetic foot ulcer.

Conclusion: The amputation status in gangrenous and non-gangrenous diabetic foot ulcer when compared, was found to be statistically significant. Though other factors like high HbA1C levels, high serum creatinine levels, low eGFR due to renal impairment in chronic kidney disease were also found to be important risk factors but they were not statistically significant. The renal function could become impaired, which could lead on to CKD in patients, presenting with diabetic foot ulcer. Therefore, special attention should be given on regular screening of diabetic patients who develop a foot ulcer. Implementing various diabetes awareness programs, taking adequate foot care, effectively managing diabetic foot ulcers could reduce the severity of complications like preventable amputations.

KEY WORDS: estimated GFR, chronic kidney disease, amputation, peripheral neuropathy, diabetic foot ulcer

INTRODUCTION:

Diabetes mellitus is a metabolic disease condition where the control of glucose levels in blood is inadequate. It has many types like type 1 DM, type 2 DM, gestational diabetes, maturity onset diabetes of the young (MODY), etc. Middle-aged along with older adults are usually affected by type 2 DM. Usually, sedentary lifestyle and dietary imbalance and choices plays an important role in its development, apart from the genetic predisposition. It affects many systems and organs including retina, kidneys, peripheral nerves. Kidney is the most important target, when we consider the microvascular damage that is seen in diabetes. When this damage happens, slowly the function of kidneys also gets disturbed.

The functioning of the kidney can be assessed by the glomerular filtration rate (GFR). Glomerular filtration rate (GFR) refers to the rate of flow of the fluid that is filtered through the glomerulus in the kidney. It can be estimated indirectly by few formulas. Hence, we call it the estimated glomerular filtration rate (eGFR). On estimation, GFR is most reliable to check the amount of the residual function of the kidneys in patients with chronic kidney disease also. Almost 50% of type 2 diabetic patients and 33.3% of type 1 diabetic patients were found to develop CKD. So, preventing and managing CKD due to impaired renal function, is important in patients with diabetic foot ulcer.

Diabetic foot (DF) can be defined as infection, ulceration, or the destruction of tissues of the foot of an individual with previously or currently diagnosed diabetes mellitus. Diabetic patients tend to develop ulceration of the foot due to peripheral sensory neuropathy. Hence, a major cause of morbidity in patients with kid-

ney failure is due to diabetic foot ulceration. This usually affects one in ten diabetics, during their life time. The high blood glucose levels often directly damage the nerves and blood vessels. If the extent of injury, due to the ulcerative lesion in diabetic foot is more, it affects the vascularity and peripheral oxygen saturation. If it becomes a non healing ulcer that causes severe damage to tissues and bone, we may need to opt for amputation of a toe, foot or a part of leg. Hence, it's important to prevent such amputations in patients with diabetic foot ulcer.

The following research aimed at analysing the demographics of the patients with diabetic foot ulcer, at seeing the extent of the injury in foot by clinical and amputation status; at studying the oxygen saturation levels in the periphery and at calculating the eGFR in patients with diabetic foot ulcer

METHODS:

It's a prospective study conducted on 80 patients with diabetic foot ulcer, who attended the Outpatient Department of Surgery in Saveetha Medical College and Hospital, a tertiary care hospital in Chennai, India during the period of January 2021 to March 2021. This study has been done after receiving the approval, by the Institutional Review of Board (IRB).

We conducted both clinical and radiological examination. Data was collected on a pre-approved proforma. A detailed history was obtained regarding the duration of the diabetes and its type. A detailed history was obtained about the mode of onset, duration and progression the foot ulcers. A detailed examination of the foot was performed and the ulcers were classified on the basis of Wagner's classifica-

tion.⁵ It is one of the most widely used and universally accepted grading systems for evaluating and managing patients with diabetic foot ulcer, consisting of six simplistic wound grades to assess ulcer depth. (Grades 0 to 5).

Grade - 0	Foot at Risk	Prevention
Grade-I	Localized, superficial ulcer	Antibiotics & glycemic control
Grade-II	Deep Ulcer to bone, ligament, or joint	Debridement, Antibiotics and glycemic control
Grade-III	Deep abscess, osteomyelitis	Debridement, some form of amputation
Grade-IV	Gangrene of toes, forefoot	Wide debridement and amputation
Grade-V	Gangrene of entire foot	Below knee amputation

Hence, we can call the diabetic foot ulcers to be gangrenous if they are of grade 4 or 5. Blood samples were taken to measure Serum creatinine, Hb and HbA1C levels. The vascularity was checked in distal pulses. The peripheral oxygen saturation in one of the toes of the affected foot was measured, except for the patients who already underwent amputation of all 5 toes as in whole forefoot or below knee or above knee amputation. We collected the X-Rays of both the foot, to check the bony involvement. We calculated eGFR through a predetermined scoring system using CKD-EPI equation.⁶ eGFR was used to determine the severity stage of CKD, that corresponds to the Kidney Disease Outcomes Quality Initiative staging.⁷

Stage 1: CKD with normal eGFR- eGFR \geq 90 mL/min per 1.73 m²

Stage 2: mild CKD- eGFR lies between 60 to 89 mL/min per 1.73 m²

Stage 3: moderate CKD- eGFR between 30 to 59 mL/min per 1.73 m²

Stage 4: severe CKD- eGFR between 15 to 29 mL/min per 1.73 m²

Stage 5: end-stage renal disease- eGFR of $<$ 15 mL/min per 1.73 m²

Our criteria for inclusion were patients with Diabetic foot ulcer of Grade I to Grade IV, who were willing to participate in the study. Patients were excluded if they were known cases of type 1 DM, acute metabolic disorders like diabetic ketoacidosis.

Data entry was executed in Microsoft Excel and data analysis was done using AnalysisToolPak add on option which is available in Microsoft Excel. Various factors that were associated with the study were analysed. The association was calculated using the Chi-square test for the qualitative data at 0.05 level of significance. The Chi-square value and P value together, further suggested if the particular association was statistically significant or not. Descriptive statistics were given in the form of frequency graphs and tables.

RESULTS:

The majority of the study participants were males- 70 (87.5 %) and only about 10 women (12.5 %). Most number of patients were belonging to stage 3 (40%) of the Wagner's diabetic foot ulcer classification, followed by stage 2 (30%), followed by stage 4 (20%), followed by stage by stage 5 (6.25%), followed by stage 1 (3.75%). [Table 1, Graph 1, Picture 1]

The patients had a mean age of 58.5 ± 9.7 years of standard deviation (range, 29 to 80 years). The duration of being affected by DM was between 2 months and 30 years (mean, 10.2 ± 6.89 years of standard deviation). Mean serum creatinine level was 1.05 ± 0.82 mg/dl (range, 0.4 mg/dL to 6.2 mg/dL). Mean HbA1C was found to be 10.2 ± 2.83 mg/dl (range, 5.8 to 16.5 mg/dL). Mean eGFR levels were found to be 103.8 ± 49.9 with a range of 10 mg/dl to 253 mg/dl. [Table 2].

Out of the 80 patients, maximum number of patients (58.7%) belonged to stage 1 CKD based on the eGFR levels, while least number of patients belonged to stage 5 (1.2%). [Graph 2]

A multifactorial comparison was done with the severity of diabetic foot ulcer, according to Wagner's classification. Around 70 patients were found to be above the age of 50. Around 65 patients in total were found to be anemic. Around 55 patients had high HbA1C values (more than 9 mg/dl). Only about 17 patients had high serum creatinine levels (more than 1.3 mg/dl). About Thirty-six patients (45.0%) underwent amputation, while the other 55% were non amputees. About 59 patients were found to have minimum of 5 years of diabetic history. Only 4 patients were in severe CKD and end stage renal disease category. About 28 patients had peripheral oxygen saturation levels less than 97. Around 59 of them were found to have non gangrenous foot ulcer, while 21 of them had gangrenous diabetic foot ulcer (stage 4 or 5). The amputation status in patients with gangrenous and non-gangrenous foot ulcer, when compared, was found to be statistically significant with chi square value of 11.1925 and p value of 0.00082 (less than 0.05), while other factors were not found to be statistically significant. [

Table 3, Graph 3]

DISCUSSION:

Diabetic foot ulcer is one of the most common complication of diabetes mellitus, which affects 15% of diabetic patients in their lifetime. Diabetic foot ulcers are main cause of hospitalization in diabetic patients and it is major cause of morbidity as patients had to undergo surgical interventions like amputations. The renal function, which is measured by the estimated glomerular filtration rate (eGFR) needs to correlated with the severity of diabetic foot ulcers, as they are an important risk factor for the need for amputations.

In such diabetic patients, chronic hyperglycaemia can often lead to impaired wound healing, due to increased susceptibility to many infections, chronic inflammatory state, diabetic micropathy and macroangiopathy, which then leads to diminished vascularity, impaired collagen synthesis, impaired autonomic dysfunction and other abnormalities in humoral mediated immunity and phagocytic functioning. 8 A high glycated haemoglobin, also impairs the endothelium mediated vasoactive responses. Shape of erythrocytes is affected by a high glucose level, making the blood more viscous, impeding the blood flow and facilitating the formation of thrombus. Thereby, increasing the risk of amputation. 9 Hence, glycaemic control is essential in healing of ulcers in diabetics 10

This present study was carried out with an aim and objective to analyse the demographics of the patients with diabetic foot ulcer, at seeing the extent of the injury in foot by clinical and amputation status; at studying the oxygen saturation levels in the periphery and at calculating the eGFR in patients with diabetic foot ulcer to correlate the stage of chronic kidney disease.

In our study, it was observed that the majority of the study participants were males- 70 (87.5 %) and only about 10 women (12.5 %). In our study, the patients had a mean age of 58.5 ± 9.7 years of standard deviation (range, 29 to 80 years). Similarly, in a study done by Shabbay et al.¹¹, the mean age was observed as 60.06.

In the study of Ahmad W et al.¹², male dominated the study population with majority within the age range of 40-70 years. In the study by Misbah Mehraj et al.¹³, males were affected more frequently with diabetic foot ulcer (66%), as compared to females (34%). Similar incidence was also seen in the study by Ali SM et al.¹⁴, as they had 65% males and 35% females. In a study done by Shabbay et al., 58.33% of patients were males.

In our study, it was observed that about 59 (73.7 %) patients were found to have minimum of 5 years of diabetic history. While in a study by Dr. Misbah et al., Duration of diabetes was greater than ten years in 58% of the patients, while 91.3% patients had diabetes of more than 5 years duration. In a study by Shabbay et al., about 56.67% of the patients had duration of diabetes for more than 5 years.

The cut off point for the diagnosis of anaemia, according to WHO, is a hemoglobin level of 12.0 g/dl for females and 13.0 g/dl for males 15,16. Diabetics have a twice more chances of developing anaemia than the non-diabetic population 16-19. In diabetic foot ulcers patients, who are anemic, the prognosis of healing of the ulcer is poor. Costa et al. had a similar finding where 89.6% of patients, who underwent amputations were anaemic and anaemia was a significant risk factor for major limb amputation 20.

In our study, it was observed that 65 patients (81.25%) were anemic. In a study done by Shabbay et al., 70% patients had a haemoglobin level below 12 g/dl with a mean haemoglobin level of 10.2

In our study, it was observed that most of the patients were belonging to stage 3 (40%) of the Wagner's diabetic foot ulcer classification, followed by stage 2 (30%), followed by stage 4 (20%), followed by stage by stage 5 (6.25%), followed by stage 1 (3.75%). While, in a study by Dr. Misbah et al, most patients belonged to Grade 4 that comprised of 34 patients, followed by Grade 2 in 22 patients, followed by Grade 3 in 16 patients. While, in a study done by Shabbay et al., Twenty-eight patients (46.67%) had Meggitt-Wagner classification grade 3.

In our study, the mean serum creatinine level was 1.05 ± 0.82 mg/dl (range, 0.4 mg/dL to 6.2 mg/dL) while the Mean HbA1C was found to be 10.2 ± 2.83 mg/dl (range, 5.8 to 16.5 mg/dL). The findings were almost similar to a study done by Sarwat Ashraf et al.²¹ on frequency of Chronic Kidney Disease in Type 2 Diabetic Patients Presenting with Diabetic Foot Ulcer, where the mean serum creatinine (mg/dl) value was reported to be 1.17 ± 0.45 while HbA1c (g/dl) of study population was found to be around 8.34 ± 0.59 . In a study done by Shabbay et al., almost two thirds of the study population i.e., 42/60(70.00%) had poor glycaemic control.

In our study, maximum number of patients (58.7%) belonged to stage 1 CKD based on eGFR values, while least number of patients belonged to stage 5 (1.2%). It's quite similar to the study results of Sarwat Ashraf et al, where maximum number of patients (48%) belonged to stage 1 CKD based on 24 Hours urinary creatinine clearance, while least number of patients belonged to stage 4 (1.2%).

The incidence of amputation is higher in diabetic foot ulcer patients who were found to have associated kidney injury such as in chronic kidney disease, when compared to the patients who did not have chronic kidney disease 22. Even the rate of healing and cure is affected if the patients also had chronic kidney disease 23. Few Studies have documented that 60-80% of the cases presenting with diabetic foot ulcers usually had CKD 24, 25.

In a study by Margolis et al.26, about 33% of the type II diabetic patients with a foot ulcer were found to have Chronic Kidney Disease. A strong association between CKD and Diabetic foot ulcer was seen with lower extremity amputation in a population based sampling of diabetic patients within the United Kingdom.

In our study, about 36 patients (45.0%) underwent amputation, while the other 55% were non amputees. About 3 patients underwent below knee amputation while only 1 patient underwent above knee amputation. Out of the 36 patients, only 5 patients were female (13.8%). The amputation status in patients with gangrenous and non-gangrenous foot ulcer, when compared, was found to be statistically significant in our study. In the study by Shabbay et al., about 51.67% of the patients underwent amputation. In the study by Dr. Misbah et al, 35 (35.0%) patients needed some sort of amputation while 5 % of patients needed multiple amputations. In their study, about 12 patients underwent below knee amputation while 10 patients underwent above knee amputations.

In the study of Viswanathan et al.27, the prevalence of foot complications such as peripheral neuropathy, peripheral vascular disease (PVD), amputations and infections were determined. The prevalence of infection was found to be 6-11% and prevalence of amputation was found to be 3% in type 2 diabetic patients. Few studies suggested that effective foot care advice should be appropriately done to reduce the burden of diabetic foot complications, especially in developing countries like India.

A multidisciplinary approach has been recommended for the adequate treatment of the diabetic foot ulcer, by means of invasive infection drainage, debridement of the necrosed areas and by starting the empirical antibiotic therapy promptly. Later, once healing is achieved, we can do an appropriately complete vascular reconstruction by plastic and vascular surgeries. Negative pressure wound therapy (NPWT) is being suggested for severe diabetic foot ulcer cases.

CONCLUSION:

A direct relationship was found between the age, gender, duration of diabetes, glycaemic control, peripheral neuropathy, grade of diabetic foot, incidence of accompanying osteomyelitis, intervention and the outcome of the disease. The amputation status in gangrenous and non-gangrenous diabetic foot ulcer when compared, was found to be statistically significant. Though other factors like high HbA1C levels, high serum creatinine levels, low eGFR due to renal impairment in chronic kidney disease were also found to be important risk factors but they were not statistically significant, due to the relatively smaller study population.

Implementing various diabetes awareness programs, taking adequate foot care, effectively managing diabetic foot ulcers with better resources for managing lifestyle is needed to decrease the negative impact of diabetes on the health and economy. The renal function could become impaired, which could lead on to CKD in patients, presenting with diabetic foot ulcer. Therefore, special attention should be given on regular screening of diabetic patients, who develop a foot ulcer.

Diabetic foot when accompanied with CKD not only limits the mobility; also affects the psychology and behaviour of diabetics negatively; thus, lowering the quality of life. Effective management of diabetic foot can reduce severity of complications like preventable amputations and possible mortality. It also improves the overall quality of living standards.

LIMITATIONS:

It has been a small scale, prospective study in only one centre. A multicentric study with larger sample size, could be followed up for a longer time in further research studies, to obtain statistically significant values.

Financial funding and sponsorship: None

Conflicts of interest: None

Ethical approval: Approved.

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